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Review Article / Artigo Revisão

Endovascular Therapy in Acute Mesenteric Ischemia

Terapêutica Endovascular na Isquemia Mesentérica Aguda

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Abstract

Background: Acute mesenteric ischemia is a cause of acute abdomen associated with high morbidity and mortality rates. Current recommendations for the initial treatment include endovascular or surgical revascularization, however they are based on small retrospective studies. The objective of this study is to review the available endovascular treatment techniques evaluating their results.
Methods: In August 2020, a survey of the last 15 years was conducted in the PubMed and EMBASE databases using the keywords "Mesenteric Ischemia [MeSH]", "Acute Disease [MeSH]", "Endovascular Procedures [MAJR]", "Thrombectomy [MeSH]" and "Thrombolysis". Review articles, systematic reviews and meta-analyses, guidelines, case studies and opinion articles, studies that did not present at least one of the intended outcomes (technical success, clinical success, recurrence rate, complications, and mortality rates) and articles on arterial mesenteric ischemia with a sample of less than 10 (n < 10) were excluded.
Results: Among 482 records initially surveyed, 19 studies were included in this review, 14 referring to arterial acute mesenteric ischemia of and 5 to venous acute mesenteric ischemia. Technical success rates ranged from 81 to 100% in arterial etiology and were 100% in venous etiology, with clinical success ranging from 53% to 71,4% in arterial etiology and between 87,5% to 100% venous etiology. Early mortality rates ranged from 9,5% to 44,7% in artery etiology and between 0% to 12,5% in venous etiology.
Conclusions: The use of endovascular techniques proved to be a viable option in the context of acute mesenteric ischemia, contributing to an improvement in the outcomes of this entity that continues to be related to a poor prognosis.

Keywords

Mesenteric ischemia [MeSH]; Acute disease [MeSH]; Endovascular procedures [MAJR]; Thrombectomy [MeSH]; Thrombolysis.

Resumo

Introdução: A isquémia mesentérica aguda é uma causa de ventre agudo associada a altas taxas de morbimortalidade. As recomendações atuais para tratamento inicial desta patologia incluem a revascularização endovascular ou cirúrgica, no entanto estas recomendações são baseadas em estudos retrospetivos com pequenas amostras. O objetivo deste trabalho é fazer uma revisão da literatura das técnicas de tratamento endovascular disponíveis, avaliando os seus resultados.
Materiais e métodos: Em agosto de 2020 foi realizada uma pesquisa dos últimos 15 anos nas bases de dados PubMed e EMBASE, com recurso às palavras-chave "Mesenteric Ischemia [MeSH]", "Acute Disease [MeSH]", "Endovascular Procedures [MAJR]", "Thrombectomy [MeSH]" e "Thrombolysis". Foram excluídos artigos de revisão, revisões sistemáticas e meta-análises, guidelines, estudos de caso e artigos de opinião, estudos que não apresentassem pelo menos um dos outcomes pretendidos (sucesso técnico, sucesso clínico, taxa de recorrência, complicações e taxas de mortalidade) e artigos referentes a isquemia mesentérica de etiologia arterial com amostra inferior a 10 (n < 10).
Resultados: De 482 registos inicialmente pesquisados foram incluídos 19 estudos nesta revisão, 14 referentes a isquémia mesentérica aguda de etiologia arterial e 5 a etiologia venosa. As taxas de sucesso técnico variaram entre 81 e 100% na etiologia arterial e foram de 100% na etiologia venosa, com sucesso clínico de 53 a 71,4% na etiologia arterial e de 87,5% a 100% na etiologia venosa. As taxas de mortalidade precoce variaram entre 9,5% e 44,7% na etiologia arterial e entre 0% a 12,5% na etiologia venosa.
Conclusão: O uso de técnicas endovasculares mostrou ser uma opção viável no contexto de isquémia mesentérica aguda, contribuindo para uma melhoria nos outcomes desta patologia que continua a estar assocada a um prognóstico sombrio.

Palavras-chave

Mesenteric ischemia [MeSH]; Acute disease [MeSH]; Endovascular procedures [MAJR]; Thrombectomy [MeSH]; Thrombolysis.

Introduction

Acute mesenteric ischemia (AMI) is a relatively rare cause of acute abdominal pain accounting to approximately 1-2% of acute abdominal emergencies[1] and less than 1 in 1000 (0.1%) of all hospitalizations.[2] This entity results from sudden intestinal hypoperfusion, which often leads to infarction of the intestinal wall with consequent intestinal necrosis. As the pathogenic mechanisms in this nosological entity are different, acute intestinal ischemia can be classified into four main subtypes according to the etiology: arterial embolism (EAMI); arterial thrombosis (TAMI); venous thrombosis (VAMI); non-occlusive (NOMI). Unlike the first three etiologies, non-occlusive mesenteric ischemia is an entity that occurs with patent arterial and venous mesenteric vasculature and is frequent in patients who present hypovolemia,

hypotension, heart failure and/or mesenteric spasm by definition. It has a greater preponderance in critically ill hospitalized individuals with severe cardiac pathology, sepsis, supportive therapy with inotropes or hemodialysis.[2,3]

AMI is a pathology that affects more the elderly patients, so the clinical presentation is in a large number of cases very nonspecific, including severe abdominal pain often reported as disproportionate to the objective examination of the abdomen. Other more frequently reported signs and symptoms are nausea and vomiting, diarrhea, hematochezia, melena, fever, abdominal distension, tachycardia or arterial hypotension.[4,5] The nonspecific clinical presentation leads to innacurate or delayed diagnosis and, despite the new advances in endovascular and surgical therapies, it can result in very high mortality rates, with approximate values of 40-80%.[6]

On blood tests, there is no specific plasmatic marker for the early detection of mesenteric ischemia, however, leukocytosis, left shift in the ratio of immature to mature neutrophils,[2] metabolic acidosis with increased anion gap, hemoconcentration and elevation of plasma levels of C-reactive protein, amylase, aspartate aminotransferase (AST) and creatine kinase (CK) are frequently documented.[1] Elevated D-dimer levels have high sensitivity in detecting mesenteric ischemia in early stages (96-100%), however they are not very specific.[7] Elevation of serum L-lactate levels reflects a more advanced stage with transmural infarction of the intestinal wall, anaerobic metabolism and necrosis of the intestinal wall, therefore it is not of interest in the early detection of ischemia, having only prognostic value insofar as its progressive clearance with successful therapy is a good independent predictor of clinical improvement.[8]

The currently most accepted complementary diagnostic test for the early diagnosis of AMI is contrast-enhanced multidetector computed tomography (CT) with an estimated sensitivity and specificity of 93.3% and 95.9%, respectively.[9] Conventional angiography is considered the gold standard for the diagnosis, however its main importance currently concerns its use in the treatment.[2,10] Multidetector contrast-enhanced CT is also a very useful exam to exclude possible differential diagnoses and to stratify the severity of intestinal ischemia according to radiological findings such as intestinal pneumatosis, presence of portomesenteric gas, densification of mesenteric adipose tissue and ascites that indicate severe ischemia and transmural infarction.[11]

The treatment of acute mesenteric ischemia includes the use of endovascular, surgical (revascularization and/or intestinal resection), hybrid techniques (retrograde open mesenteric stenting – ROMS) techniques or just medical treatment, depending on the etiology and the specific clinical and imaging characteristics of each patient. The currently existing recommendations and guidelines are essentially based on retrospective studies with small samples and case studies, lacking published randomized and controlled trials in order to guide the treatment in this specific pathology.[12,13] Available endovascular techniques include mechanical percutaneous thrombectomy or by thrombus aspiration, percutaneous transluminal balloon angioplasty (PTA)/stenting, infusion of fibrinolytics and/or vasodilators.

The aim of this study is to carry out a literature review of endovascular treatment modalities for acute mesenteric ischemia, evaluating their technical and clinical efficacy, incidence of complications, recurrence rate and early and long-term mortality rates.

Materials and Methods

The search was carried out in August 2020 using the PubMed and EMBASE databases using the keywords "Mesenteric Ischemia [MeSH]", "Acute Disease [MeSH]", "Endovascular Procedures [MAJR]", "Thrombectomy [MeSH]" and "Thrombolysis". The search algorithms used in each database are included in Annex 1. The adopted inclusion criteria are related to the language (English, Portuguese and Spanish), species (human) and date of publication in the last 15 years (from 2006 to 2020). Review articles, systematic reviews and meta-analyses, guidelines, case studies and opinion articles were excluded. Studies that did not present at least one of the intended outcomes (technical success, clinical success, recurrence rate, complications and mortality rates) were excluded. From articles referring to mesenteric ischemia of arterial etiology, studies with a sample smaller than 10 ($n < 10$) were excluded, while in articles referring to mesenteric ischemia of venous etiology, no lower sample limit was applied.

Data extraction from the selected articles was initially performed dividing the studies into the group of patients with acute mesenteric ischemia of arterial etiology and patients with acute mesenteric ischemia of venous etiology. The extracted data refers to the following variables: type of study, date of publication, sample size, mean age of the sample, etiology of occlusion, affected vessels, type(s) of endovascular treatment(s) instituted, technical success, clinical success, recurrence rate, complications, early and late mortality rates and interventions after endovascular treatment (laparotomy, laparoscopy and intestinal resection). Additional data from patients exclusively submitted to non-endovascular treatments (systemic and/or surgical) or with chronic mesenteric ischemia (CMI) were excluded, being the data collected only from samples of patients with acute mesenteric ischemia submitted to at least one endovascular technique.

Technical success is defined as the restoration of arterial/venous flow without the need for surgical or endovascular reintervention. Clinical success is defined as the resolution of the clinical signs and symptoms after treatment in each study. Complications reported per study concern preferably to those imputed only to endovascular treatments, unless these are inseparable from complications of other previous or subsequent treatments. Early mortality is defined as death within 30 days and/or during hospitalization due to treatment failure, treatment-related complications (ischemic, hemorrhagic, inflammatory, infectious, and others) or the presence of other comorbidities. Long-term mortality adds deaths documented by follow-up after hospital discharge to early mortality.

Results

In the initial search, 521 results were found, 325 in the PubMed database and 196 in the EMBASE database, from which 39 duplicates were excluded. With the application of the inclusion criteria described above, the relevant articles were subsequently selected, using the analysis of titles and abstracts, making a total of 49 potentially eligible articles for this review.

After a more detailed analysis, 19 studies were selected to be included in this review, 14 referring to acute mesenteric ischemia of arterial etiology and 5 referring to acute mesenteric ischemia of venous etiology. Of the 30 excluded

studies: 8 had a sample below the limit (n < 10), 7 had only results from the hybrid technique, 3 had only results from surgical treatment, 3 had joint results from multidisciplinary approaches, 2 had joint results from AMI and CMI treatment, 2 addressed the risk of using contrast in computed tomography (CT), 1 only evaluated prognostic factors, 1 evaluated the results of laparotomy timing, 1 only evaluated hospitalizations and costs, 1 evaluated the prevalence of use of different therapeutic modalities and 1 presented results of treatment with systemic fibrinolysis. Figure 1 illustrates the article selection diagram. Tables 1 and 2 summarize the data extracted from the articles referring to mesenteric ischemia of arterial etiology and mesenteric ischemia of venous etiology, respectively.

Figure 1 – Illustrative diagram of study selection. Adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

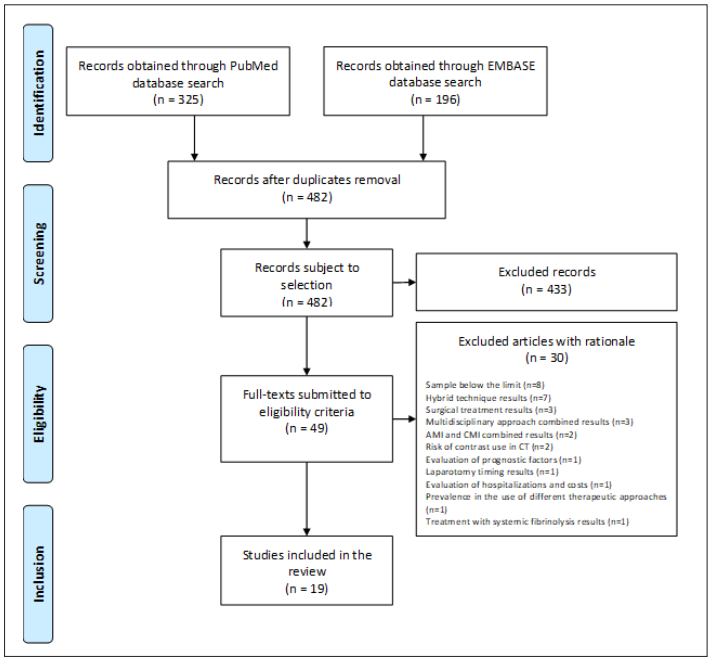

Table 1 – Data from studies referring to acute mesenteric ischemia of arterial etiology

Study	Year	Sample (n)	Mean age (years)	Etiology			Arteries involved	Primary treatment				Secondary treatment			
				Embolic	Thrombotic	Other		Pharmacological thrombolysis	Mechanical thrombectomy	Thrombus aspiration	PTA/Stent	Pharmacological thrombolysis	Mechanical thrombectomy	Thrombus aspiration	PTA/Stent
Freitas B (14)	2018	20	69.8	17 (85%)	2 (10%)	NK- 1 (5%)	SMA - 17 (85%) SMA + InfMA - 1 (5%) SMA + other - 2 (10%)	0	20 (100%)	0	0	4 (20%)	0	2 (10%)	PTA - 7 (35%) Stent - 5 (25%)
Zhang Z (15)	2017	18	60.2	15 (83.3%)	3 (16.6%)	0	SMA (mt) - 14 (77.8%) SMA (pb) - 1 (5.6%) SMA (mt+pb) - 3 (16.6%)	18 (100%)	0	0	0	0	0	9 (50%)	PTA - 2 (11.1%) Stent - 1 (5.6%)
Forbrig R (17)	2017	19	69 (50-88)	0	19 (100%)	0	SMA - 16 (84.2%) SMA + CTr - 2 (10.5%) SMA + InfMA - 1 (5.3%)	0	0	0	Stent - 19 (100%) 22 arteries (100%)	0	0	0	Double stent- 4/22 arteries (18%)
Paetzel C (23)	2016	38	78 (44-88)	NS	NS	NS	SMA - 28 (100%)	NS							
Arya S (18)	2016	11	69.7	0	11 (100%)	0	SMA - 5 (45.5%) SMA + CTr - 3 (27.3%) CTr - 2 (18.2%) InfMA - 1 (9.1%)	0	0	0	11 (100%)	NS	NS	NS	NS
Raupach J (16)	2016	37	75,5 (51-93)	37 (100%)	0	0	SMA - 37 (100%)	0	0	37 (100%)	0	2 (5.4%)	0	0	PTA + Stent - 2 (5.4%)
Eslami MH (24)	2016	990	68.5 (18-97)	NS	NS	NS	NS	NS							
Branco BC (25)	2015	27	72.3 (19-89)	NS	NS	NS	NS	12 (44.4%)	0	0	15 (55.6%)	NS			
Karkkainen JM (19)	2015	50	81 (59-94)	18 (36%)	0	0	SMA - 12 (66.7%) SMA + CTr and/or InfMA – 6 (33.3%)	0	0	17 (94.4%)	1 (5.6%)	4 (22.2%)	0	0	3 (16.7%)
			78 (58-92)	0	32 (64%)	0	SMA - 3 (9.4%) SMA + CTr and/or InfMA – 29 (90.6%)	0	0	3 (9.4%)	29 (90.6%)	0	0	0	3 (9.4%)
Beaulieu RJ (26)	2014	165	NE	NS	NS	NS	NE	NS							
Jia Z (27)	2014	21	71 (54-87)	NS	NS	NS	SMA (mt) - 17 (81%) SMA (pb) - 4 (19%)	0	0	21 (100%)	0	14 (66.7%)	0	0	Stent - 1 (4.8%)
Arthurs ZM (20)	2011	56	65	28%	72%	0	SMA - 66% SMA + CTr - 34%	48%	11%	NS	32%	0	Post thrombolysis in 12% of the group	NS	Post thrombolysis in 33% of the group Post mechanical thrombectomy in 22% of the group
Block TA (21)	2010	42	77 (59-82)	12 (28,6%)	26 (61.9%)	NK 2(4.8%) Arterial dissection - 1(2.4%) Stent thrombosis - 1(2.4%)	SMA - 42 (100%)	13 (31%)	2 (4.8%)	3 (7.1%)	Anterograde pathway - 20 (47.7%) Retrograde pathway - 4 (9.5%)	NS			
Acosta S (22)	2009	21	78 (62-90)	10 (47.6%)	0	0	SMA - 10 (100%)	0	0	9 (90%)	0	3 (30%)	1 (10%)	0	Stent - 1 (10%) SMA proximal dissection
			68 (53-81)	0	11 (52.4%)	0	SMA - 11 (100%)	0	0	0	Anterograde pathway - 7 (63.6%) Retrograde pathway - 3 (27.3%)	1 (9.1%)	0	1 (9,1%)	0

Caption: SMA - superior mesenteric artery; InfMA – inferior mesenteric artery; CTr – celiac trunk; mt – main trunk; pb – peripheral branch; ROMS – retrograde open mesenteric stenting; NK – not known; NS - not specified

Table 1 (cont.) – Data from studies referring to acute mesenteric ischemia of arterial etiology

Technical success	Clinical success	Complications	Early Mortality	Long term mortality	Interventions after endovascular treatment			
					Laparotomy	Laparoscopy	Bowel resection	Surgical revascularization
20 (100%)	NS	Minor arterial perforations - 2 (10%)	8 (40%)	11 (55.5%)	14 (70%)	NS	14 (70%)	0%
Complete - 8 (44.4%) Partial - 10 (55.6%)	NS	Respiratory failure - 3 (16.7%) Acute kidney injury - 1 (5.6%)	3 (16.7%)	4 (22.2%)	6 (33.3%)	NS	6 (33.3%)	NS
21/22 arteries (95%)	10 (53%)	Improper implantation of 2 stents in the SMA instead of the CTr - 1 (5.3%)	8 (42%)	NS	7 (36.8%)	NS	4 (21.1%)	NS
37 (97.4%)	NS	NS	17 (44.7%)	NS	NS	NS	NS	1 (2.6%)
11 (100%)	NS	Multiorgan failure - 3 (27.3%) Postoperative sepsis - 5 (45.4%)	5 (45.4%)	NS	7 (63.6%)	NS	4 (36.4%)	NS
34 (91.9%)	NS	Bleeding from fatal jejunal vessel injury - 1 (2.7%) Minor inguinal hematoma - 3 (8.1%) Post catheterization pseudoaneurysm - 1 (2.7%) Peripheral embolization (renal artery and common femoral artery)- 2(5.4%)	10 (27%)	NS	27 (73%)	NS	15 (40.5%)	1 (2.7%)
NS	NS	NS	15.30%	NS	NS	NS	9%	0%
NS	NS	Acute kidney injury - 2 (7.4%) Pneumonia - 6 (22.2%) Sepsis - 7 (25.9%) Surgical site infection - 5 (18.5%) Thromboembolic events - 1 (3.7%)	6 (22.2%)	NS	11 (40.7%)	NS	11 (40.7%)	0%
17 (94%)	NS	Bleeding from brachial artery - 1 (5.6%) Distal branch dissection of the SMA - 1 (5.6%)	7 (39%)	10 (55.6%)	5 (27.8%)	NS	5 (27.8%)	0%
27 (84.4%)	NS	Bleeding from femoral artery - 1 (3.1%) Dissection and perforation InfMA - 1 (3.1%) Stroke - 1 (3.1%)	9 (28.1%)	11 (34.4%)	15 (46.9%)	NS	12 (37.5%)	3 (9.4%)
NS	NS	NS	24.9%	NS	NS	NS	14.4%	NS
Complete - 6 (28.6%) Partial - 15 (71.4%)	15 (71,4%)	NS	2 (9.5%)	2 (9.5%)	5 (23.8%)	NS	5 (23.8%)	0%
87%	NS	Acute kidney injury - 27% Respiratory failure - 27% Acute myocardial infarction - 2% Gastrointestinal bleeding - 7% Bleeding at the puncture site - 9% Stroke - 2%	50%	NS	69%	NS	58%	13%
NS	NS	NS	10 (24%)	16 (38%)	23 (55%) 12 of these (31%) with second-look surgery	NS	8 (19%)	NS
Complete - 1 (10%) Partial - 6 (60%)	NS	SMA dissection - 2 (20%) of which proximal - 1 (10%) Residual emboli in peripheral vessels - 6 (60%)	1 (10%)	2 (20%)	7 (70%)	1 (10%)	3 (30%)	1 (10%) - no endovascular treatment
Complete - 8 (72.7%) Partial - 2 (18.2%)	NS	Residual emboli in peripheral vessels - 2 (18.2%)	2 (18.2%)	3 (27.3%)	7 (63.6%)	0%	4 (36.4%)	3 (27.3%) – Only ROMS

Table 2 – Data from studies regarding acute mesenteric ischemia of venous etiology

Study	Year	Sample (n)	Average age (years)	Veins involved	Treatment modality				Technical success
					Pharmacological thrombolysis	Mechanical thrombectomy	Thrombolysis + Thrombectomy	PTA/Stent	
Rabuffi P (28)	2020	8	56.5 (37-81)	SMV - 1 (12.5%); SMV + PV - 1 (37.5%); SMV + PV + SV - 4 (50%)	0	0	8 (100%)	0	8 (100%)
Yang S (29)	2016	15	44.1	SMV - 5 (33.3%); SMV + PV - 6 (40%); SMV + PV + SV - 4 (26.7%)	15 (100%) *	0	0	0	Complete thrombus lysis - 12 (80%) Partial thrombus lysis - 3 (20%)
Wichman HJ (30)	2014	8	53 (24-74)	SMV - 3 (37.5%); SMV + PV - 3 (37.5%); SMV + PV + SV - 2 (25%)	1 (12.5%)	2 (25%)	2(25%)	Primary or additional treatment - 8 (100%) SMV - 2 PV - 1 SMV + PV - 4 SMV + PV + SV - 1	8 (100%)
Yang S (31)	2014	13	43.33	SMV + PV (more common)	13 (100%)	0	0	0	Complete thrombus lysis - 11 (84.6%) Partial thrombus lysis - 2 (15.4%)
Wang MQ (32)	2011	12	41.2 (18-75)	SMV – 12 (100%)	0	0	12 (100%)	0	12 (100%)

Caption: SMV - superior mesenteric vein; PV – portal vein; SV – splenic vein; IJV – internal jugular vein; * - Treatment performed after intestinal resection by laparotomy in all patients; ARDS – acute respiratory distress syndrome; NS - not specified

Acute mesenteric ischemia of arterial etiology

From the 14 studies analyzed, data were collected corresponding to a total of 1551 participants. The mean age of patients in each study ranged from 60.2 to 79 years.

Embolic etiology was more prevalent in 3 publications,[14-16] while thrombotic etiology was more prevalent in 6 publications.[17-22] The prevalence of each etiology was not scrutinized in 5 publications.[23-27] Block et al.[21] also reported a case of AMI due to arterial dissection and another due to thrombosis of a previously placed stent.

The artery most often involved was the superior mesenteric artery (SMA) and its peripheral branches, and in 6 studies[15,16,21-23,27] it was the only artery involved in all patients in the sample. Other arteries involved included the inferior mesenteric artery (InfMA) and the celiac trunk (CTr) to a lesser extent.

In the study by Zhang Z et al.[15] catheter-guided pharmacological thrombolysis was instituted as the primary treatment in all patients; in the study by Freitas B et al.[14] percutaneous mechanical thrombectomy was used with a rotational device – 6F Rotarex® S Debulking Device (Straub Medical , Wangs, Switzerland), in the studies by Raupach J et al.[16] and Jia Z et al.[27] thrombectomy by aspiration of the thrombus through a catheter was performed and in the study by Forbrig R et al.[17] percutaneous transluminal angioplasty (PTA)/Stent was used. In the remaining publications, combinations of the various endovascular techniques were used, excluding 3[23,24,26] in which the instituted techniques are not reported.

In 4 studies[14,15,18,27] 100% technical success was achieved. In the remaining studies technical sucess was 97.4%,[23] 95%,[17] 91.9%,[16] 88%,[19] 87%[20] and 81%.[22] Clinical success was reported in two publications with values of 71.4%[27] and 53%.[17]

The most frequently reported complications directly associated with endovascular treatments were minor arterial perforation 10%;[14] hemorrhage at the puncture site 4%[19] and 9%;[20] hematoma at the puncture site 8.1%;[16]

Table 2 (cont.) – Data from studies regarding acute mesenteric ischemia of venous etiology

Clinical success	Recurrence	Complications	Early Mortality	Long term Mortality	Interventions after endovascular treatment		
					Laparotomy	Laparoscopy	Bowel resection
7 (87.5%)	Recurrent thrombosis of IJV - 4 (50%)	Superior epigastric artery hemorrhage - 1 (12.5%) Multiorgan failure - 1 (12.5%)	1 (12.5%)	1 (12.5%)	0%	0%	0%
14 (93.3%)	1 (6.7%)	Sepsis - 2 (13.3%) Abdominal compartment syndrome - 1 (6.7%) Arrhythmia - 1 (6.7%) Pneumonia - 3 (20%) ARDS - 2 (13.7%) Acute kidney injury - 4 (26.7%) in need of hemodialysis - 2 (13.7%) Abdominal hemorrhage - 3 (20%) Minor hemorrhage - 3 (20%) Local infection - 2 (13.3%)	1 (6.7%)	1 (6.7%)	3 (20%)	NS	2 (13.3%)
7 (87.5%)	1 (12.5%) - 14 months after initial treatment	Splenic hemorrhage - 1 (12.5%) Mesenteric vein perforation - 1 (12.5%)	1 (12.5%)	2 (25%)	NS	NS	NS
13 (100%)	0%	Hemorrhage - 3 (23.1%) Acute kidney injury - 2 (15.4%)	0%	1 (7.7%)	4 (30.8%)	4 (30.8%)	4 (30.8%)
12 (100 %)	0%	Minor hematoma at IJV puncture site - 3 (25%) Minor hemorrage at IJV puncture site - 1 (8.3%)	0%	0%	NS	NS	0%

formation of peripheral residual emboli 38.1%;[22] improper implantation of stents 5.3%;[17] pseudoaneurysm formation after catheterization 2.7%;[16] fatal hemorrhage from jejunal vessels 2.7%;[16] dissection of the proximal SMA 4.8%[22] and distal branches 2%[19] and 4.8%;[22] dissection and perforation of the InfMA 2%[19] and formation of peripheral emboli in large caliber arteries (common femoral artery and renal artery) 5.4%.[16] Other reported complications concern not only to the endovascular treatments performed, but also to subsequent surgical treatments such as respiratory failure 16.7%[15] and 27%;[20] acute kidney injury 5.6%,[15] 7.4%[25] and 27%;[20] surgical site infection 18.5%;[25] pneumonia 22.2%;[25] sepsis 45.4%[18] and 25.9%;[25] acute myocardial infarction 2%;[20] stroke 2%;[19,20] other unspecified thromboembolic events 3.7%;[25] gastrointestinal bleeding 7%[20] and multiorgan failure 27.3%.[18]

Early mortality rates varied greatly from study to study, with a minimum value of 9.5%[27] and a maximum of 44.7%.[18] Long-term mortality varied between 9.5%[27] and 55.5%.[14]

Regarding reported interventions after endovascular treatment, the need for laparotomy varied between 23.8%[27] and 73%,[16] only the study by Acosta S et al.[22] reports the use of laparoscopy in 1 case (10%) in the subgroup of patients with AMI of embolic etiology. The need for intestinal resection after endovascular treatment varied between 9%[24] and 70%[14] and in relation to the need for surgical revascularization after endovascular treatment (excluding data from Acosta S et al.[22] in which not all patients underwent non-hybrid percutaneous treatment) ranged from 0%[14,24,25,27] to 13%.[20]

Acute mesenteric ischemia of venous etiology

In 5 analyzed publications, data were collected from 56 patients with a mean age between each study of 41.2 to 56.5 years.

The most frequently involved vein was the superior mesenteric vein, being the only vein involved in all cases in the study by Wang MQ et al.[32] In the remaining publications, there were cases in which the portal vein and/or splenic vein were concurrently involved.

Direct (percutaneous transhepatic/intrahepatic transjugular) or indirect (through the superior mesenteric artery) catheter-guided pharmacological thrombolysis was the technique used in all patients in the publications by Yang S et al.,[29,31] and in the 2016 study[29] the indirect route was the only one used. In the studies by Rabuffi P et al.[28] and Wang MQ et al.,[32] catheter-guided pharmacological thrombolysis was used only via the direct route in combination with percutaneous mechanical thrombectomy with thrombus aspiration. In the study by Wichman HJ et al.[30] all patients underwent stenting of at least one vessel, additionally, in some patients, catheter-guided pharmacological thrombolysis and/or percutaneous mechanical thrombolysis with thrombus aspiration were also used.

Technical success of 100% was achieved in all studies, however, partially in the studies by Yang S et al. in 20%[29] and 15.4%[31] of the patients. Two publications reported clinical success of 100%,[31,32] one 93.3%[29] and two 87.5%.[28,30] Reported recurrence rates were 0%,[31,32] 6.7%,[29] 12.5%[30] and 50%.[28]

Complications associated with endovascular treatments were reported, such as hemorrhage at the puncture site of the internal jugular vein 8.3%;[32] hematoma at the puncture site of the internal jugular vein 25%;[32] mesenteric vein perforation 12.5%;[30] superior epigastric artery hemorrhage 12.5%;[28] splenic vein hemorrhage 12.5%[30] and other unspecified hemorrhages 20%[29] and 23.1%.[31] Other reported complications concern not only the endovascular treatments performed, but also the subsequent surgical treatments, including sepsis 13.3%;[29] arrhythmia 6.7%;[29] acute respiratory distress syndrome 13.3%;[29] pneumonia 20%;[29] abdominal compartment syndrome 6.7%;[29] acute kidney injury 26.6%[29] and 15.4%[31] requiring hemodialysis 13.3%;[29] abdominal hemorrhage 20%;[29] surgical site infection 13.3%[29] and multiorgan failure 12.5%.[28]

Early mortality rates were 0%,[31,32] 6.7%[29] and 12.5%.[28,30] The long-term reported mortality was 0%,[32] 6.7%,[29] 7.7%,[31] 12.5%,[28] 25%.[30]

After endovascular treatment, the need for laparotomy was reported in 0%,[28] 20%[29] and 38%[31] of the cases, laparoscopy in 0%[28] and 30.8%[31] and intestinal resection in 0%,[28,32] 13.3%[29] and 30.8%.[31]

Discussion

Acute mesenteric ischemia of arterial etiology

Acute mesenteric ischemia of arterial origin can be classified according to its etiology into embolic and thrombotic. The embolic cause is the most frequent with a prevalence of 30-50% of cases of AMI and the most frequent embolic source is cardiac, being associated with ischemic or structural heart disease, heart valve disease, infective endocarditis and atrial fibrillation.[1,10] The thrombotic cause is implicated in approximately 15-35% of cases of AMI[2,10] and this is also more frequently associated to occlusions of proximal SMA near the arterial ostium comparing to emboli, due to its close relationship with atherosclerotic phenomena more frequent at this level.[1,10] In the treatment of embolic AMI, open surgical embolectomy is usually the indicated procedure; however, if there is no evidence of intestinal necrosis requiring intestinal resection, endovascular techniques may be attempted primarily, whereas in thrombotic AMI, endovascular techniques should be used initially (more commonly PTA/Stent, with the possibility of selecting other techniques such as mechanical thrombectomy by aspiration of the thrombus and catheter-guided fibrinolysis) in all patients who do not show evidence of intestinal necrosis.[12]

The primary use of percutaneous balloon angioplasty (PTA)/stent was the method of choice in patients with AMI of thrombotic etiology, being the main treatment modality in the study by Forbrig et al.[17] and in the subgroups of AMI of thrombotic etiology from the studies by Kärkkäinen JM et al.[19] and Acosta S et al.[22] In these cases, the technical success rates were high [95%,[17] 84%[19] and 100%[22]], early mortality was higher in the study by Forbrig et al.[17] compared to the remaining [42%,[17] 28.1%[19] and 18.2%[22]], with reported long-term mortality rates overlapping between studies [34.4%[19] and 27.3%[22]]. The use of laparotomy was more prevalent in the study by Acosta S et al.[22] [36.8%[17] vs 46.9%[19] vs 63.6%[22]], with higher intestinal resection rates in publications by Kärkkäinen JM et al.[19] and Acosta S et al.[22] [21.1%,[17] 37.5%[19] and 36.4%[22]].

Comparing the endovascular treatment modalities in patients with AMI of embolic etiology, the following stand out: a) thrombectomy by catheter-guided thrombus aspiration in the studies by Raupach J et al.,[16] by Jia Z et al.[27] and in the AMI subgroups of embolic etiology in the studies by Kärkkäinen JM et al.[19] and Acosta S et al.;[22] b) mechanical thrombectomy in the study by Freitas B et al.;[14] and c) catheter-guided pharmacological thrombolysis in the study by Zhang Z et al.[15]

The technical success reported in studies with mechanical thrombectomy and catheter-guided thrombolysis was higher [100%[14,15]] than in studies with aspiration thrombectomy [100%,[27] 91.9%,[16] 94%[19] and 70%[22]]. Early mortality was higher in the study using mechanical thrombectomy 40%[14] and lower in two studies using aspiration thrombectomy 9.5%[27] and 10%.[22] However, in the remaining two studies using aspiration thrombectomy higher early mortality rates were reported 27%[16] and 39%.[19] In the study using catheter-guided thrombolysis, early mortality was 16.7%.[15] The long-term mortality rate was higher in the study using mechanical thrombectomy and in one of the studies using aspiration thrombectomy [55.5%[14] and 55.6%[19]], in the remaining studies and in the study resorting to catheter-guided thrombolysis the reported long-term mortality rates were more favorable [9.5%,[27] 20%[22] and 22.2%[15]].

The rate of laparotomy was higher in the study using mechanical thrombectomy and in 2 using aspiration thrombectomy [70%,[14] 73%[16] and 70%[22]], the remaining studies using thrombectomy by aspiration and the catheter-guided thrombolysis study showed lower rates of laparotomy [27.8%,[19] 23.8%[27] and 33.3%[15]]. The intestinal resection rate was significantly higher in the study using mechanical thrombectomy 70%[14] when compared to the remaining [33.3%,[15] 40.5%,[16] 27.8%,[19] 23.8%[27] and 30%[22]].

Results of primary endovascular treatments were compared to results of surgical treatment (surgical revascularization) in seven studies.

Zhang Z et al.[15] compared results among 12 patients submitted to endovascular therapies and 18 patients submitted to surgical therapy, endovascular therapies showed the need for a smaller extent of intestinal resection on average (88±44 vs 253±103 cm, p= 0.01), and no significant differences were found in 30-day mortality nor the need for secondary laparotomy.

In the study by Arya S et al.[18] no significant differences were observed between both groups (11 patients with endovascular treatment and 23 with surgical treatment) in terms of complications, morbidity and mortality.

Eslami MH et al.[24] in a multicenter study with data between 2003 and 2011 from the North American database NIS (National Inpatient Sample) which involved 990 patients undergoing endovascular treatment and 573 undergoing surgical treatment, concluded that despite the increased frequency of use of endovascular therapies in AMI, no statistically significant changes in long-term mortality from AMI were demonstrated. However, in-hospital mortality (15.3% vs 21.9%, p=0.01), need for intestinal resection (9% vs 14.9%, p<0.001), length of hospital stay (p<0.001) and median hospitalization costs ($73317 vs $101762, p<0.001) were significantly lower in the endovascular treatment group despite higher Elixhauser comorbidities index (3±0.1 vs. 2.7±0.1 p=0.008).

Another multicenter study by Branco BC et al.[25] using the North American database NSQIP (National Surgical Quality Improvement Program) with data from patients between 2005 and 2010, compared 3 groups [27 patients with endovascular treatment, 23 with hybrid treatment (retrograde open mesenteric stenting - ROMS) and 389 with surgical treatment] and concluded that the group submitted to endovascular therapies had a lower 30-day mortality (22.2% vs 34.8% vs 40.4% p=0.049). There was a trend towards a lower occurrence of complications such as pneumonia and sepsis, as well as a lower need for transfusions of packed red blood cells, although not in a statistically significant way. No significant differences were found in terms of the need for intestinal resection, secondary laparotomy and length in hospital stay.

Beaulieu RJ et al.[26] using data from the US database NIS (National Inpatient Sample) between 2005 and 2009, performed a comparison between 2 groups (165 patients undergoing endovascular treatment and 514 undergoing surgical treatment). Mortality 24.9% vs 39.3% (p=0.01), mean duration of hospital stay 12.9 vs 17.1 days (p=0.006), need for intestinal resection 14.4% vs 33.3 % (p<0.001) and need for total parenteral nutrition 24.4% vs 13.7% (p=0.025) were lower in the endovascular group.

In the publication by Arthurs ZM et al.,[20] the outcomes of 56 patients submitted to endovascular techniques and 14 submitted to surgical therapy were compared, with the group submitted to endovascular techniques having lower rates of laparotomy (69% vs 100% p<0, 05), less extent of necrotic bowel resection [median and interquartile range (IQR): 52 cm (11-140 cm) vs 160 cm (90-250 cm), p<0.05],

lower incidence of acute kidney injury (27% vs 50%, p<0.05) and respiratory failure (27% vs 64%, p<0.05). In general mortality, no significant differences were observed, however, in the subgroup of AMI of thrombotic etiology, mortality was lower in the group submitted to endovascular therapy [odds ratio (OR): 0.1, 95% CI of 0.1-0, 76, p<0.05].

A multicenter study by Block TA et al.[21] using the Swedish database Swedish Vascular Registry (Swedvasc) analyzed and compared data from 121 patients who underwent surgical revascularization and 42 patients who underwent endovascular procedures between 1999 and 2006. The endovascular group showed lower rates of laparotomy (55% vs 100%, p<0.001), lower rate of intestinal resection (19% vs 63%, p<0.001), lower incidence of short bowel syndrome (27% vs 55%, p =0.009) and less need for second-look laparotomy (31% vs 67%, p<0.001). The 30-day (24% vs 42%, p=0.03) and 1-year (38% vs 59%, p=0.02) mortality was significantly lower in the endovascular group, as well as the estimated long-term mortality (p=0.02).

Acute mesenteric ischemia of venous etiology

Acute mesenteric ischemia of venous etiology/mesenteric venous thrombosis represents 5-15% of cases of mesenteric ischemia.[2,10] This entity can be idiopathic or secondary in most cases (90%) to hypercoagulable states such as thrombophilia and neoplasms, cirrhosis and portal hypertension, inflammatory abdominal diseases such as pancreatitis, diverticulitis and infectious/inflammatory pathology of the biliary tract.[2,10] Treatment involves systemic anticoagulation with unfractionated heparin; in patients with no clinical improvement, it may be necessary to use more invasive treatments such as surgical or endovascular thrombectomy, systemic or catheter-guided pharmacological thrombolysis.[12,13]

Comparing the outcomes of the studies included in this review, Rabuffi P et al.[28] and Wang MQ et al.[32] report on the entire sample the combined use of mechanical thrombectomy with thrombus aspiration and catheter-guided pharmacological thrombolysis, Yang S et al.[29] and Yang S. et al.[31] report the isolated use of catheter-guided pharmacological thrombolysis, noting that in the 2016 study by Yang S. et al.[29] all patients were primarily submitted to emergent intestinal resection, so it is not possible to compare the data with the remaining studies accurately. In the study by Wichman HJ et al.[30] the treatment which all patients underwent was stenting ± primary balloon angioplasty, resorting to the other techniques in 62.5% of patients.

The technical success in the four studies was 100% and the clinical success was maximum (100%) in the study by Yang S et al.[31] and in the publication by Wang MQ et al.,[32] in the remaining ones it was 87.5%(28.30). Rabuffi P et al.[28] presented the highest recurrence rate, which was lower in the study by Wichman HJ et al.[30] (12.5%) and in the remaining ones was 0%.[31,32] In the latter, early mortality was more favorable [0%[31,32]] compared to the publications by Wichman HJ et al.[30] and Rabuffi P et al.[28] (12.5%). Long-term mortality was higher in the study using stenting [25%[30]] and lower in one of the studies using mechanical thrombectomy + thrombolysis [0%[32]]. In the others it was 12.5%[28] and 7.7%.[31] Only the study with the isolated use of pharmacological thrombolysis reports the need to employ other interventions after endovascular treatment, with 30.8% of patients undergoing laparotomy and subsequent intestinal resection and another 30.8% undergoing laparoscopy.[31]

In the 2016 study by Yang S. et al.,[29] the outcomes of a group of 15 patients were evaluated on which treatment with pharmacological thrombolysis was performed, guided by a catheter placed in the superior mesenteric artery (urokinase 100,000 IU bolus + 600,000 IU/day + papaverine 120 mg/day up to 72 hours after surgery, then low molecular weight heparin (LMWH) 80UI/kg/dosage, twice daily), this time after open thrombectomy and emergent intestinal resection, comparing with another group of 17 patients in which only systemic anticoagulation is used postoperatively (low molecular weight heparin (LMWH) 80UI/kg/dosage, twice a day 12 hours after surgery). It was concluded that the catheter-guided thrombolysis group had a higher rate of complete thrombus removal (80% vs 29.4% vs p = 0.001), less need for second-look laparotomy (20% vs 70.6%, p=0.001) and of new posterior intestinal resection (13.3% vs 58.8% p=0.002), as well as consequently a lower incidence of short bowel syndrome (6.7% vs 41.2%, p=0001). The 30-day (6.7% vs 41.2%, p=0.001) and 1-year (52.9% vs 93.3%, p=0.014) mortality were significantly lower in the catheter-guided thrombolysis group. The difference in incidence rates of abdominal bleeding requiring surgical intervention and transfusion of packed red blood cells was not statistically significant between the two groups.

The 2014 study by Yang S. et al.[31] aimed to evaluate the initial treatment with the best results in patients with AMI due to superior mesenteric vein thrombosis with circumscribed peritonitis and suspected intestinal necrosis. Outcomes of a group with 12 patients who were primarily undergoing emergent surgical exploration (open thrombectomy and/or intestinal resection) were compared with another group of 13 patients who were undergoing catheter-guided pharmacological thrombolysis via percutaneous transhepatic/transjugular intrahepatic or via superior mesenteric artery (urokinase 100,000 IU bolus + 200,000/300,000 IU/day ± papaverine 120 mg/day). In both groups, patients were anticoagulated with oral fondaparinux sodium 5 mg/day and intravenous argatroban 80 mL/day. The group undergoing catheter-guided thrombolysis had a shorter mean duration of hospital stay (20.46 ± 6.59 days vs 43 ± 13.77 days, p<0.001), shorter time period for symptoms remission since admission (7.23 ± 2.42 days vs 18.25 ± 7.69 days, p<0.001), earlier oral/enteral nutrition replacement (8.92 ± 1.89 days vs 20.5 ± 5.13 days, p<0.001), shorter bowel extension resections (29.23 ± 50.24 cm vs 170.83 ± 61.27 cm, p<0.001) and lower total hospitalization costs (72785.6 ± 21828.16¥ vs 2000020.4 ± 91505.62¥, p=0.001). No statistically significant differences were observed between the two groups in rates of morbidity, 30-day mortality, and 1-year mortality.

Limitations

One of the limitations of this review is related to the fact that the analyzed studies were entirely retrospective (based on a single center or multicenter) and with small samples, which showed great heterogeneity between the endovascular techniques used, their use in an isolated or combined way depending on its availability/clinical status of each patient and drugs administered [example: alteplase (rtPA)/urokinase (uPA)] and in some publications there is no data concerning the therapeutic modalities used. Therefore, with the data from available studies, it is not possible to compare in a highly reliable way the outcomes associated to each endovascular technique individually, due to the lack of large-scale studies comparing the different techniques individually.

Another limitation is related to the comparison of surgical revascularization results with endovascular techniques, insofar as in-hospital management protocols for patients with AMI show some heterogeneity. In some cases, it is possible that there is a selection bias with the use of endovascular techniques to the detriment of surgical revascularization in patients with greater comorbidities who are not candidates for surgery. From another point of view, it can also be noticed that in the case of patients in worse clinical status with longer duration of ischemia, and a greater probability of intestinal necrosis, there is a higher chance that surgical treatment is proposed in detriment of more conservative techniques.

Conclusion

Taking into account the available evidence, it is possible to conclude that the increasing use of endovascular techniques in the treatment of acute mesenteric ischemia of arterial and venous etiology contributes to the improvement of outcomes associated with this pathology, which continues to be associated with a poor prognosis.

These more conservative treatment modalities are especially relevant in patients with a prompter diagnosis. In these situations, there is a greater probability of success for endovascular therapies, obviating surgical treatments, namely in an emerging context, with high rates of morbidity and mortality.

Annex 1 - Search algorithms used:

- PubMed: ((Mesenteric Ischemia AND acute) AND endovascular) OR ((“Mesenteric Vascular Occlusion/therapy”[MAJR]) AND “Acute Disease”[MeSH Terms]) OR (“Mesenteric Ischemia”[MeSH Terms] AND “Endovascular Procedures”[MAJR] AND “Acute Disease”[MeSH Terms]) OR (“Mesenteric Ischemia”[Mesh] AND acute[All Fields] AND (thrombolysis[All Fields] OR ((“fibrinolytic agents”[Pharmacological Action] OR “fibrinolytic agents”[MeSH Terms] OR (“fibrinolytic”[All Fields] AND “agents”[All Fields]) OR “fibrinolytic agents”[All Fields] OR “thrombolytic”[All Fields]) OR thrombolytic’[All Fields] OR thrombolytic,[All Fields] OR thrombolytica[All Fields] OR thrombolyticagents[All Fields] OR thrombolytical[All Fields] OR thrombolytically[All Fields] OR (“fibrinolytic agents”[Pharmacological Action] OR “fibrinolytic agents”[MeSH Terms] OR (“fibrinolytic”[All Fields] AND “agents”[All Fields]) OR “fibrinolytic agents”[All Fields] OR “thrombolytics”[All Fields]) OR thrombolyticum[All Fields] OR thrombolyticus[All Fields]) OR (“thrombectomy”[MeSH Terms] OR “thrombectomy”[All Fields]) OR (“suction”[MeSH Terms] OR “suction”[All Fields] OR (“mechanical”[All Fields] AND “aspiration”[All Fields]) OR “mechanical aspiration”[All Fields]))) AND (English[lang] OR Portuguese[lang] OR Spanish[lang]) AND “humans”[MeSH Terms].
- EMBASE: (‘mesenteric blood vessel occlusion’/exp OR ‘mesenteric ischemia’/exp) AND acute:ab,ti AND endovascular:ab,ti OR (‘mesenteric ischemia’:ab,ti OR ‘mesenteric vascular occlusion’:ab,ti) AND acute:ab,ti AND endovascular:ab,ti AND ([english]/lim OR [portuguese]/lim OR [spanish]/lim) AND ([article]/lim OR [article in press]/lim OR [data papers]/lim OR [short survey]/lim).

Ethical disclosures / Divulgações Éticas

Conflicts of interest: The authors have no conflicts of interest to declare.

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Confidentiality of data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Confidencialidade dos dados: Os autores declaram ter seguido os protocolos do seu centro de trabalho acerca da publicação dos dados de doentes.

Protection of human and animal subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Protecção de pessoas e animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial.

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